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NOTE ON THE OCCURRENCE OF LEISHMAN-
DONOVAN BODIES IN "CACHEXIAL FEVERS"
INCLUDING KALA-AZAR

Leonard ROGERS

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many of the girls is the chief cause of the curvature of the spine, and that it calls very strongly for more attention to physical education, and especially for more provision for gymnastics than is found at present in elementary schools for girls. Girls, too, of the lower classes do not as a rule play the same vigorous games as do the boys, or as are played now by girls of the higher classes of society.

Eyes.—There was no case of colour blindness or even of "confusion of colours" among the girls.

Acuteness of Vision.—Out of the total number, 202, nearly 13 per cent. had errors of refraction requiring the use of glasses. Only 39 per cent. of these were already provided with any glasses.

Hearing.—Out of 1,400 cases 117, 8.3 per cent., had defective hearing to some extent. In 80 of these the defect was slight, a watch normally heard at 18 in. being audible at distances varying from 6 in. to 12 in. In 37 cases the defect was considerable, the watch being heard only at less than 6 in., in many cases at less than 2 in. In nearly all these, however, one ear only was affected. In several there was a history of otorrhoea. In no case was the deafness noticeable in ordinary conversation. Contrary to my expectation I found but few of the cases of defective hearing associated with enlarged tonsils or adenoids, they were 13 in all, or about 11 per cent.

Throat and Nose.—Enlarged tonsils, adenoids, or both, were found in 148 cases, nearly 10 per cent. Many of the cases were slight and no treatment was advised. Fifteen cases of adenoids were recommended to undergo an operation. The association with deafness was, as remarked above, very small, being limited to 13 cases. The percentage of enlarged tonsils and adenoids was very much less in the girls than the boys, namely, 10 per cent. instead of 34 per cent. It may be suggested that cases were allowed to pass undetected in the former, but I do not think that this was the case. There was undoubtedly a striking absence among the scholarship girls of the facial signs of adenoids so common in our elementary schools and especially so in the classes for mental defectives—but there too I think more frequent on the whole in boys than girls.

Urine.—Among the 1,580 cases examined 151, or nearly 10 per cent., had albuminuria. This percentage is almost exactly the same as that found among the boys. Only those cases are included in which there was both a distinct cloud on boiling and a definite ring on treatment with cold nitric acid. The amount of albumen varied from a slight cloud to, in a few cases, as much as one-fifth solid albumen. In as many cases as possible the urine was examined a second time at a few days' interval: 82 cases were thus re-examined, in 67 albumen was present on both occasions. I have endeavoured as far as possible to keep the albuminuria cases under continued observation. This has not been always easy, as they are under no obligation to attend any subsequent examination, and opportunities for further investigation can only be obtained as a favour. I have, however, succeeded in making over 300 examinations of the urine in old cases.

Seventy-Three Cases were Examined Three Times.—In 180 (83 per cent.) of the examinations albumen was found. In 9 cases albumen was present at every examination.

Forty-One Cases were Examined Four Times.—Albumen was found in 93 of the examinations (76 per cent). In 10 cases there was albumen at every examination.

Fourteen Cases were Examined Five Times.—In 57 of the examinations (81 per cent.) albumen was found. In 6 cases albumen was present on each occasion.

The longest time any case has been under observation is five years; 23 cases have been under observation for periods of from three to five years. Of these 23, 10 had albuminuria at every examination, 12 had no albuminuria the last time they were examined (3 of these also had none the last time but one), 1 case was found to have no albuminuria at an intermediate examination, but albumen was present again when last she was seen. The amount of albumen was found to vary a good deal in the same individual at different times. On the whole, the tendency certainly was for the amount to diminish at each subsequent examination, but this was by no means invariably the case.

Causation of the Albuminuria and Health of the Girls.—The majority of these girls were of good general appearance, several were indeed among those who were noted as being specially robust and healthy-looking; 10 were somewhat anaemic, and were among those who were classed as delicate. Albuminuria is said to be common in children of a neurotic temperament, subject to night terrors, somnambulism, or other symptoms of an unstable nervous system.

Certainly by far the larger number of the girls I examined were by no means of this type.

There was a history of scarlet fever or diphtheria in a certain number of cases, but not in a greater proportion than among the whole number of girls examined. In no case was any history of kidney disease given, and in none had the existence of any kidney trouble been suspected. I did not find among them any cases with further symptoms of kidney disease or circulatory disturbance. Enlarged tonsils were present in somewhat greater proportion than among the girls in general, but not to any great extent.

In a few of the cases where the amount of albumen was largest a microscopic examination of the urine was made. No casts were found. I have not as yet found evidence of deterioration of the general health among the girls who have been kept under observation. One girl has had scarlet fever since she was first examined, and informs me she was then told that it was complicated by inflammation of the kidneys. As she appears to have been but slightly ill, the diagnosis was probably due to the pre-existing albuminuria.

The conclusions I have drawn from the very imperfect observations I have been able to make are as follows:

1. In the majority of the cases in which albuminuria was found the condition was not merely accidental and transitory, but was more or less permanent, at any rate for a few years.

2. I find no evidence of consequent deterioration of health so far as I have been able to watch the cases.

3. On the whole the albuminuria tends to diminish, and in more than half the cases had disappeared when they were last seen.

Unfortunately the time during which it has been possible to keep the girls under observation is too short to throw much light on the subject of the ultimate prognosis in these cases of albuminuria. That some will result in nephritis is probable, but the large number of cases in which the albumen has disappeared after persisting for some months or years certainly appears to me to afford some evidence against the theory that albuminuria in the apparently healthy is to be considered in all, or nearly all cases, an early stage of interstitial nephritis. It is, of course, impossible to say that some of the albumen may not have been due to leucorrhoea. The urine in all the cases reported was, however, quite clear, and there was no signs of leucorrhoeal discharge—cases in which there was merely a faint trace of albumen present were on this account not included.

As regards the condition of the girls generally as brought out in these examinations, I think this may be considered satisfactory. The girls as a rule were healthy. Although a considerable proportion might have been better developed in many ways, and a variety of defects were discovered, these were generally not serious, and the falling below the standard of health was not great. The candidates were the picked scholars of the elementary schools; they had all worked hard, and had had to pass a fairly severe competitive examination. The medical examination was interesting in regard to the question as to whether such application to work had injured the health of the scholars, an accusation not infrequently made concerning work in Board schools. In the case of those who came before me—the girls who succeeded—I think the answer was in the negative.

NOTE ON THE OCCURRENCE OF LEISHMAN-DONOVAN BODIES IN "CACHEXIAL FEVERS," INCLUDING KALA-AZAR.

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THE work of Donovan¹ in showing the above parasite-like bodies to be commonly present in chronic fevers in Madras, following very closely on the first description of them by Leishman,² has raised the very important question as to whether some of the cases hitherto known as "malarial cachexia," including the Assam epidemic form of the disease kala-azar, might not be caused by the new parasite. On my recent return to India I was fortunate enough to be placed on special duty to inquire into the prevalence of fevers in Dinaipur (which is one of the districts in which I showed some years ago³ that the Assam epidemic fever took its origin in the early Seventies, owing to five out of six successive years of deficient rainfall). I have, therefore, been able to examine for the new parasite by spleen puncture, with some

results which appear worthy of record. As my object was to find out how to differentiate the cases with the new bodies from chronic malarial fevers, all cases with enlargement of the spleen below the ribs and recent fever were submitted to the little operation, which was rendered painless by spraying the skin first with ethyl chloride. Although, in all, 30 cases were examined in this way in small dispensaries no ill result followed. The duration of the cases varied from one month to several years, as will be seen from the following table, most of them presenting very marked enlargement of the spleen, accompanied by darkening of the skin, anaemia, and considerable emaciation; that is the typical picture of "malarial cachexia." In short, these were just the cases which I pointed out some years ago as individually considered indistinguishable from kala-azar in Assam, but which differ from that disease, when the family histories are gone into, in that more than 1 death in a family within a year or two is very exceptional in the sporadic form seen in Lower Bengal; while it is the rule in the epidemic form of Assam, where among the patients in a large dispensary three-quarters had lost half, or more than half, of their household from the disease.⁴ Further, in the worst part of the Dinajpur districts I could obtain no evidence of villages being decimated by the disease, and of the people deserting them, as always occurred in the affected tracts in Assam. Yet, given a single case of the two forms, there is no means of distinguishing them, except, perhaps, by the greater rapidity of the occurrence of the markedly cachexial stage in the epidemic form.

With regard to the present series of cases, malignant tertian malarial parasites were found in some, Leishman-Donovan's bodies in others, while in the remainder no parasites could be detected, although in most a film prepared from the peripheral blood was examined, as well as those of the spleen blood, Romanowsky and Leishman's stains being used. It will be most convenient to tabulate, for purposes of comparison, the two series of cases in which parasites were found. The negative cases, which constituted just one half (15 out of 30) were precisely similar in nature to those given in the tables.

Table of Cases in which Parasites were Found.

I.—FEVERS SHOWING LEISHMAN-DONOVAN BODIES.

No.	Sex.	Age.	Duration of Fever.	Present Fever.	Anaemia.	Skin.	Spleen.	Liver.	Wasting.	Parasites.
1	F.	4	15 months	Daily	Very marked	Dark	A.S.S.	1"	Very marked	Numerous.
2	M.	15	1 year	Daily	Marked	Very dark	Beyond navel	1"	Very marked	Scanty.
3	M.	25	2 years	Slight	Slight	Dark	"	Nil	Slight	Numerous.
4	M.	15	7 months	Daily	Slight	Dark	Beyond navel	Nil	Very marked	Scanty.
5	M.	40*	2 years	Daily	Slight	"	"	Nil	Thin	Numerous.
6	M.	14	1 month	Daily	Slight	Nil	To navel	1"	Nil	Scanty.
7	M.	7	1 year	Daily	Very marked	Nil	To navel	1"	Very marked	Scanty.
8	F.	7	1 month	Daily	Marked	Dark	Beyond navel	3"	Thin	Numerous.
9	F.	6	1 year	Daily	Slight	Nil	A.S.S.	4"	Extreme	Scanty.
10	M.	8	1 year	Nil lately	Marked	Dark	A.S.S.	1"	Very marked	Scanty.

II.—FEVERS SHOWING MALARIAL PARASITES.

1	M.	7	3 years	Slight	Slight	Very dark	Beyond navel	Nil	Thin	Mal. tert.
2	M.	7	2 years	Frequent	Slight	Very dark	A.S.S.	1"	Thin	Mal. tert.
3	M.	12	2½ years	Daily	Marked	Dark	To navel	1"	Thin	Mal. tert.
4	M.	14	2 years	Daily	Marked	Nil	Beyond navel	Nil	Nil	Mal. tert.
5	M.	8	3½ years	Frequent	Very marked	Dark	A.S.S.	1"	Thin	Mal. tert.

A.S.S. means down to the anterior superior spine of the ilium. " equals 1 in. below the edge of the ribs.

* Died of pneumonia. Bodies found in the spleen, liver, and bone marrow.

A study of the above table shows that there is no point of marked difference between the two series, for in both the majority of the cases occurred in children and were of a chronic type, the malarial ones happening to show this in the more marked degree on the average, while the darkening of the skin since the onset of the fever—a point on which the relatives sometimes volunteered information before they were asked—the marked enlargement of the spleen, and to a less degree, of the liver, the anaemia and wasting are all common to both series. The area in which these cases were examined is but a little south of the Darjeeling terai, and is very malarious, the spleen rate in the villages from which most of these cases came having been 99 and 100 per cent., while it was in this very tract of country that the Malarial Commission found a very definite relationship to exist between the spleen rate and malarial endemic index, so that there can be no doubt as to the prevalence of malaria in this part. It is also remarkable that even with spleen puncture no parasites of any kind were found in half the cases, although in all but 3 of the 15 negative cases fever was still occurring regularly, while they had not been recently dosed with quinine. Most of the cases in both series showed an increase of the large mononuclear

white corpuscles, and also a large proportion of lymphocytes and a reduced one of polynuclears, just as I have previously shown occurs in chronic malarial fevers as well as in cases of "malarial cachexia" and kala-azar, so that if the new bodies are not a form of malarial organism then it is evident that a large mononuclear increase is not diagnostic of malaria, but rather of an indication of the presence of a protozoal, as opposed to a bacterial, invasion of the system. It is disappointing to find that even spleen puncture fails to differentiate all the chronic fever cases, but better results may be obtained by repeating the procedure, as a second puncture was successful in one case.

It is, of course, conceivable that all these chronic cases may be due to the new parasite-like bodies, and the presence of malarial parasites in many of them also may be a coincidence. If the new parasites do not form melanotic pigment, then it is clear that the great majority of these chronic cachexial fevers are complicated by malaria, for I have shown on more than one occasion that both in kala-azar and also in "malarial cachexia," as seen round Calcutta, recent black pigment is nearly always met with in the liver, spleen, etc. after death; while during the occasional high rises of temperature which occur during the course of the low fever of the cachexia stage of the disease malarial parasites can frequently be found. On the other hand, against the view that the new bodies are a late secondary infection frequently occurring in the subjects of chronic malarial fever are the facts that these new parasites were found after only one month's fever in two of the cases recorded above; while it will be shown presently that they are also to be met with in fairly early stages of kala-azar; so that, on the whole, it appears to be more likely that they are a new form of protozoa very closely allied to the malarial parasites, and producing a very similar train of symptoms, but with a greater tendency to bring about a cachexial state very rapidly, and a greater resistance to the action of quinine in small doses. In view of the above results, it is clear that the differentiation of the new fever from chronic malaria by purely clinical means apart from spleen puncture, will be an extremely difficult

matter, and will require a far larger series of cases than present one. Yet if the new bodies prove to be the cause of all the chronic fevers in which they are met with a great advance will have been made, and a new field of research opened up.

LEISHMAN-DONOVAN BODIES IN KALA-AZAR.

In December last a letter appeared in the *Indian Medical Gazette* from Major Donovan pointing out that the cases which he had found the new parasites resembled kala-azar closely in type, and suggesting that the latter disease might also be due to them. Ross has also made a similar suggestion. Thanks to the kindness of my old friend Dr. D. Price, of the Nowgong district of Assam (whose experience of kala-azar is absolutely unrivalled at the present time), sending me slides made from blood obtained during the spleen puncture in seven cases of undoubted kala-azar, the duration of which varied from five months to two years and a half, I have been able to search for the new bodies. The results may be very briefly summarized by saying that numerous Leishman-Donovan's bodies were readily obtained in three of the cases, while in two more they were

sparingly met with. In one case none could be found, but the notes of the case reported that the patient was improving and was expected to recover. In the remaining case the slide was spoilt in trying a new fixing agent. Since these results were obtained, Dr. Bentley of Assam has announced in the *Indian Medical Gazette* that he has also found these bodies in kala-azar cases, and has therefore abandoned his recently-expressed Malta fever theory of the disease which I showed was based on serum tests with too low dilutions to be of any value, while in two series of cases I got partly negative results, since which similar negative reactions have been obtained at the Army Medical School laboratory in another series of kala-azar bloods sent by Dr. Price. These parasites, then, are certainly to be found in kala-azar, and should they prove to be the actual cause of this disease the matter will be one of great practical importance, for the measures recommended by me, and very successfully carried out by Dr. Dodds Price and others, both for the suppression of the disease by segregation measures,¹⁰ and ¹¹, and the very marked lowering in the mortality produced by more efficient treatment with quinine, should be equally valuable in the treatment of the sporadic form of the affection. Still more important from this point of view is the demonstration beyond the possibility of dispute by Dr. Price¹² of the certain action of quinine as a prophylactic against kala-azar, for when he first put into operation the segregation measures he lost hospital assistants and menials of the infected camp from the disease with great regularity, until he started, now several years ago, dosing them all regularly with quinine, since which he has not lost one, except a man who had already contracted the disease before this measure was started. A drug which is such a perfect prophylactic can hardly fail to have some curative action, although it often fails in advanced cases, and must be pushed in early ones to be effective, as I urged several years ago in my original report on the disease. I lay stress on this point because Major Donovan says that quinine is of little use in the disease. Now that we have a method of diagnosing the affection in the earlier stages quinine should be pushed as soon as possible before the patient reaches a cachexial state, and his total leucocytes, and still more the phagocytic polynuclears, are reduced to but a small fraction of their proper numbers, as I have previously pointed out, is so commonly the case in the most hopelessly of these chronic fevers,⁴ and ⁶.

With regard to the bodies themselves, I can find no difference between those seen in the sporadic form in Dinajpur, and also quite recently in Calcutta in cases admitted to the Medical College Hospital as "malarial cachexia," and those I have found in kala-azar, while both agree clearly with specimens kindly shown me by Major Leishman in London, and sent me by Major Donovan from Madras, as well as those depicted by Manson and Low still more recently in a case from Sylhet.⁷ In view of the great differences of opinion as to the nature of the parasites among leading medical authorities, it is useless to add any more to those already expressed, especially as further forms doubtless remain to be discovered before the life-history of the organism can be made out fully. That an asexual form of sporulation goes on in the spleen appears certain, but more than that I am not prepared to say at present. Nothing resembling an adult trypanosoma has yet been seen.

I have also recently visited the Kola-Lukh area but found the outbreak had died out, only recovering cases being seen. It is worthy of note that nearly all the Dinajpur cases were found only about forty miles from the Kola-Lukh area. I would also like to point out that the discovery of a slightly different form of protozoan parasite than the present known malarial ones in both "malarial cachexia" and kala-azar does not *per se* clear up the mystery of the origin of the spreading epidemic form of the disease in Assam from the endemic form in Lower Bengal.

In my original report I stated that I had expected to have met with a different form of plasmodium from those of ordinary malarial fevers, and for this purpose examined a series of cases of commencing fever in kala-azar-infected houses so as to get them in the earliest stages, but failed to find any differences in the parasites met with in the peripheral blood from those of malaria (spleen puncture, unfortunately, not having been done), except in kala-azar they "appeared to be less frequently pigmented, but the difference was not sufficiently striking to allow of there being differentiated by it." Further, "I never came across any crescent forms." If the new organisms are piroplasma, as suggested by Laveran, then some of the parasites I saw in

the peripheral blood may be an intracorporeal form of the parasite, although many of them were undoubtedly pigmented malarial organisms, which were met with throughout every stage of the disease in different cases, although often absent for a considerable time during the occurrence of the low form of fever in individual instances. In several of the Dinajpur cases recently examined the peripheral blood has showed unstained amoeboid-like bodies, usually situated in red corpuscles, which present a purple stippling with Leishman's stain, the exact nature and significance of which I am uncertain about. As I worked in Assam mainly with unstained specimens fixed with osmic acid vapour (Romanowsky and Leishman's stains not then being in general use), some of the intracorporeal unpigmented forms then seen may possibly have been of this nature.

Of the forms met with in blood withdrawn from the spleen during life, the commonest is a small oval body slightly longer than it is broad and measuring about one-third the diameter of a red blood corpuscle in its longest axis. It has two nuclei, one of which is small and often rod-shaped and stains deeply, while the other is larger, more rounded, and less darkly stained. They are usually situated opposite each other, close to the capsule and in close contact with each other. These bodies are free in the blood and may be very scanty, but in cases with actual fever when the blood is obtained they are not infrequently very numerous, being met with in numbers in a single field of the microscope. In addition to this form, small groups of similar bodies are met with clumped together so as to closely simulate a quartan sporulating malarial parasite, while in others these are seen in the act of breaking up into the small forms. A still earlier stage of this sporulation is seen in which pairs of unequal-sized nuclei are grouped within a single cell, but no signs of subdivision are yet apparent. These last forms are somewhat larger than the longest of the single forms, and appear to be produced by a subdivision of the nuclei of the latter. I have not yet found this form in the peripheral circulation, but possibly it may be present in small numbers. I have also seen them within polynuclear white corpuscles, where they may show degenerative changes.

In conclusion, I would suggest as a suitable provisional term for the chronic fevers showing Leishman-Donovan bodies in the spleen the term "cachexial fever" until further advances allow of a more accurately descriptive name being agreed upon.

NOTE.—Since this paper was written it has been pointed out by the editor of the *Scientific Memoirs of Army Medical Officers* that the bodies recently described by Majors Leishman and Donovan were first recognized and described by Lieutenant-Colonel D. D. Cunningham, I.M.S., as occurring in Delhi boil as long ago as 1885 in a paper in Part I of the *Scientific Memoirs*. If these bodies are to be called by any one's name it should, therefore, be by that of Cunningham.

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THE LEISHMAN-DONOVAN BODY.

BY
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So far the peculiar parasites associated with splenomegaly in India and other places have been found in the spleen, liver, and bone marrow, in the former two by puncture during life, and in all three *post mortem*. Lately having made sections of some of the other organs of a case which died of kala-azar in the wards of the London School of Tropical Medicine, and which presented many Leishman-Donovan bodies in the spleen, liver, and bone marrow, we have found the same parasite in the lymphatic glands from the mesentery.

Sections of the pancreas, kidney, and large and small intestine have so far shown nothing.

We record this fact now as it may be of importance in the further elucidation of the disease. We hope to publish shortly a full account of the case with photographs, and details of the arrangement of the parasites in the different organs.



